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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Rouli Zhou

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EXAMINER

GUSSOW, ANNE

ART UNIT

PAPER NUMBER

1643

MAIL DATE

DELIVERY MODE

01/28/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/540,539	Applicant(s) ZHOU ET AL.	
	Examiner ANNE M. GUSSOW	Art Unit 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 November 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 16-21 is/are pending in the application.
- 4a) Of the above claim(s) 7-11, 14 and 17-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 12, 13 and 16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>11/10/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. No claims have been amended.

Claim 15 has been cancelled.
2. Claims 7-11, 14, and 17-21 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 13, 2007.
3. Claims 1-6, 12, 13, and 16 are under examination.

Rejections Maintained

Claim Rejections - 35 USC § 101 and 112, First Paragraph

4. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.
5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.
6. The rejection of claims 1-6, 12, 13, and 16 under 35 U.S.C. 101 and 35 U.S.C. 112, first paragraph is maintained.

The response filed November 10, 2009 has been carefully considered but is deemed not to be persuasive. The response states that LAPTM4B has been demonstrated to play pivotal roles in tumorigenesis, tumor growth and metastasis in the instant invention. The specification discloses that both mRNA level and the LAPTM4B-35 protein level of LAPTM4B are up-regulated in the majority of hepatocellular carcinoma tissues by experiments, such as, Northern Blot (see Fig. 1A) and in situ hybridization for mRNA (Fig. 2A), and immuno-histochemistry (see Fig. 2B), immuno-cytochemistry. ((See Fig. 2C) and Western Blot (.see Fig. 3) for protein (see page 3, line 30 to page 4, line 2; Shao et al. *Oncogene.*, 2003, 22(32): 5060-5069; Liu et al. *World J. Gastroenterol.* 2004, 10(11): 1555- 1559; Peng et al. *World J. Gastroenterol.* 2005, 11 (18): 2704-2708). The upregulated LAPTM4E-35 protein level is related with many cancers and its magnitude is positively correlated with hepatocellular carcinoma grades and negatively correlated with hepatocellular carcinoma differentiation, implicating the close relationship between LAPTM4B and HCC. (See page 4, lines 12-16, 16-28 and Fig. 1C and Fig. 17; see also Shao et al. *Oncogene.*, 2003, 22(32): 5060-5069; Peng et al. *World J. Gastroenterol.* 2005, 11(i 8): 2704-2708; Zhou et al. *European Journal of Cancer*, 43 (4): 809- 8t5; Zhou et al. *Cancer Letter*, 264(2): 209-217; Yang et al. *Oncology Reports*, 2008, July, accepted). Furthermore, the inventors have recently demonstrated that the high level of LAPTM4B-35 in HCC is also correlated positively with the presence of tumor thrombin in portal vein (metastasis in liver) and adversely with the survival period (.prepared manuscript to Hepatology). Therefore, the correlation between the up-regulation of LAPTM4B and clinical malignance of patients with HCC

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and some other cancers indicates the specific and substantial utility of LAPTM4B as a novel marker in cancer diagnosis and prognosis. For example, primers and probes having a segment of the nucleotide sequence of SEQ ID Nos: 1-3, 6 and 8, and antibodies directed to LAPTM4B polypeptides can be utilized to determine its expressive level in the biological samples (see Fig. 8, Shao et al. *Oncogene.*, 2003, 22(32): 5060~5069; Liu et al. *World J. Gastroenterol.* 2004, 10(11): 1555-1559; Peng et al. *World J. Gastroenterol.* 2005, 11(18): 2704-2708; Zhou et al. *European Journal of Cancer*, 43 (4): 809- 815; Zhou et al, *Cancer Letter*, 264(2): 209-217; Yang et al. *Oncology Reports*, 2008, July, accepted; and also unpublished data in the inventor's lab). See response pages 5-10.

In response to this argument, while the examiner agrees that one of ordinary skill in the art would be able to produce the molecules of SEQ ID Nos. 1-4, 6, and 7, applicant's disclosure has not provided evidence that each of these sequences is found in cancer cells. Applicant's specification discloses that SEQ ID No. 4 is encoded by SEQ ID No. 1 (page 3, lines 14-15) thus providing support for the cancer related polynucleotide of SEQ ID No. 1 and the encoded polypeptide of SEQ ID No. 4. The specification discloses the detection of SEQ ID No. 6 in PCR cloning, thereby providing support for the nucleotide allele of SEQ ID No. 6. The specification does not disclose detection of SEQ ID Nos. 2-3 or 7 in either normal or cancerous cells. There was no evidence provided that these polynucleotides and polypeptide exist naturally, or are cancer-related. Therefore, the polynucleotides are not cancer related and the polypeptide is a totally new, uncharacterized polypeptide with no well-established utility.

Therefore after a fresh consideration of the claims and the evidence provided the rejection is maintained.

Conclusion

7. No claims are allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
January 26, 2009

/David J Blanchard/
Primary Examiner, Art Unit 1643